

ANNEX A

Filename: ProteOptics Microfluidics specifications 1.1.doc
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Subject:
Author: Ariel Lipson
Keywords:
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ProteOptics Microfluidics Specifications

ProteOptics is developing a biochip and optical system for monitoring protein-protein interactions. The chip, which is made from glass or plastic, has a thin layer of gold to which proteins are immobilized. The microfluidics system is designed to create a crisscross of channels that will enable the immobilization procedure and thereafter measure their interaction with another set of proteins.

A microfluidics system is to be developed in order to deliver minute amounts of fluid (buffer and sample) to the surface of the chip. Figure 1 shows an illustration of the biochip and microfluidic cover.

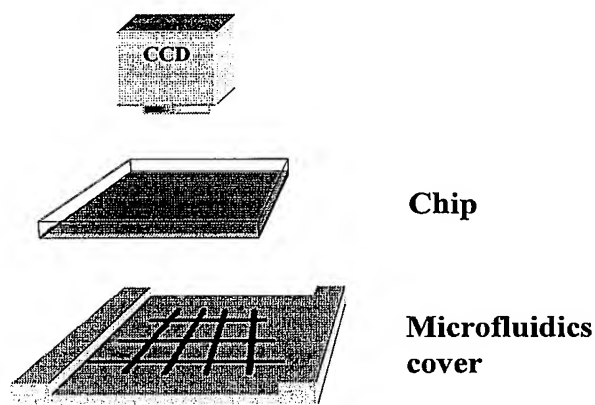


Fig 1: Schematic illustration of the biochip and microfluidics cover. The actual configuration of the channels and ports is defined in the following figures.

Specifications of the microfluidic system:

1. Disposable technology – We intend the microfluidic cover (and its valves) to be disposable. This in turn demands a low cost technology and design. The disposable technology should enable at least a 1 day experiment, at least 100 operations of each valve and a total of 10-100ml of fluid running in the channels at a flow rate of about 10 μ l/min.
2. The general configuration of the microfluidic system is 8x8 channels forming a crisscross (Figure 3). This will enable 64 measurement spots for up to 16 different substances. The flow of the liquid in each channel is straight, meaning that there should be no leakage from one channel to the other. Two main possibilities for creating the crisscross:
 - a. Two sets of 8 channels or one that can be rotated 90 degrees.
 - b. One complex system with valves that can manipulate the flow path to receive the desired crisscross and withstand the experiment procedure (next item).
3. To fully understand the system it is best to review a typical experiment:

Immobilization

- a. An 8 channel microfluidics system is placed or operated on the optical chip (Figure 2).



- b. Working on a single channel, the user flows a buffer solution for a couple of minutes (up to tens of minutes) until system is stable. The user can set and control the flow rate.
- c. Meanwhile an autosampler prepares the injected sample (quantity and temperature)
- d. At a desired instance, the buffer flow is **instantly** (<1 sec) switched to the prepared sample solution, keeping the same flow rate.
- e. When the sample is fully injected the flow of buffer is **instantly** returned.
- f. There should be **minimal mixing** between the buffer and sample.
- g. The user repeats these steps on all 8 channels to create the immobilized protein layer. Each channel will be addressed only once.
- h. If technology permits:
 - i. There is no prevention (and will be preferred) from working on all **channels simultaneously**. This will reduce the stabilization time considerably.
 - or**
 - ii. The buffer solution only flows in all channels simultaneously and the sample is injected separately to each channel. This will reduce the stabilization time considerably and allow individual treatment for each sample.

Analyte Injection

- i. A set of new 8 channels is set to cross the 8 immobilized strips of proteins (Fig 3). This could be accomplished, for example, by rotating the microfluidics system right angle or by having a set of valves that control the channel pattern.
 - j. The same procedure as in the immobilization part is repeated for each channel.
 - k. When all channels are completed we receive 64 interaction spots.
4. Dimensions:
- a. The sampling area of the chip is about $5 \times 5 \text{ mm}^2$ (red rectangle in figures 2-3).
 - b. Channels are $(100-150) \mu\text{m} \times (10-50) \mu\text{m}$ (W x H).
 - c. Spacing between channels is about $300 \mu\text{m}$.
 - d. Size of cover is yet to be determined but should be in the range of a few centimeters.
5. If valves are used they should be actively controlled, with dead volumes less than $1 \mu\text{l}$ and switching time of about 0.5sec or less. They should withstand pressures of about 1atm.
6. A syringe and Teflon tubing is proposed to deliver the fluids to the chip. We intend an automated system to connect the tubing to the input and output ports. Therefore the ports should be designed for this purpose. There should be no leakage at these ports for 1atm pressure.
7. The microfluidic cover can be a separate part from the glass biochip to allow future positioning of proteins on the surface using an external arrayer. There should be no leakage of fluids around the channels. The placement of the channels on the arrayed proteins should be exact and have a tolerance of about $100 \mu\text{m}$.



8. Flow rates of 1-30ul/min will be applied. Samples of up to 100ul will be injected in between the continuous flow of buffer.

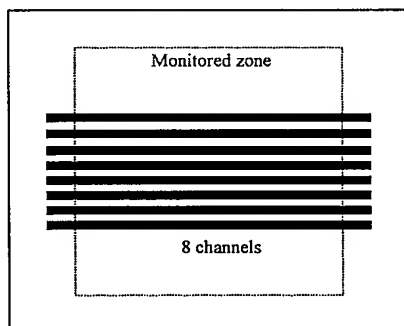


Fig 2: 8 channels are placed on the optical chip. The whole red zone in monitored.

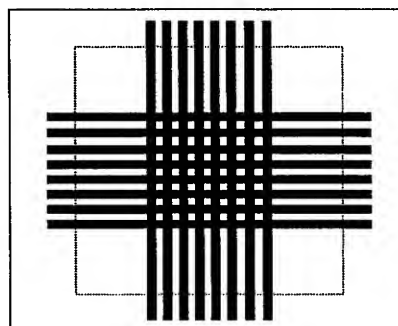


Fig 3: Another set of 8 channels (or using a valve controlled system) is set across the previous protein strips to form a crisscross pattern, with 64 interaction points.